Normal IgH Repertoire Diversity in an Infant with ADA Deficiency After Gene Therapy.

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Public Summary:
Abstract Purpose: Adenosine deaminase (ADA) deficiency causes severe combined immunodeficiency (SCID) through an accumulation of toxic metabolites within lymphocytes. Recently, ADA deficiency has been successfully treated using lentiviral-transduced autologous CD34+ cells carrying the ADA gene. T and B cell function appears to be fully restored, but in many patients' B cell numbers remain low, and assessments of the immunoglobulin heavy (IgHV) repertoire following gene therapy are lacking. Methods: We performed deep sequencing of IgHV repertoire in peripheral blood lymphocytes from a child following lentivirus-based gene therapy for ADA deficiency and compared to the IgHV repertoire in healthy infants and adults. Results: After gene therapy, Ig diversity increased over time as evidenced by V, D, and J gene usage, N-additions, CDR3 length, extent of somatic hypermutation, and Ig class switching. There was the emergence of predominant IgHM, IgHG, and IgHA CDR3 lengths after gene therapy indicating successful oligoclonal expansion in response to antigens. This provides proof of concept for the feasibility and utility of molecular monitoring in following B cell reconstitution following gene therapy for ADA deficiency. Conclusion: Based on deep sequencing, gene therapy resulted in an IgHV repertoire with molecular diversity similar to healthy infants.

Scientific Abstract:
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